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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/521,936

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EXAMINER

HILL, KEVIN KAI

ART UNIT

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/521,936	<b>Applicant(s)</b> KAMINSKI, JOSEPH M.	
	<b>Examiner</b> KEVIN K. HILL	<b>Art Unit</b> 1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 20 April 2009.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-6, 15, 18-20 and 23-26 is/are pending in the application.
- 4a) Of the above claim(s) 2-4, 19 and 24-26 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1, 5, 6, 15, 18, 20 and 23 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                       | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>April 21, 2009</u> .  | 6) <input type="checkbox"/> Other: _____                          |

## **Detailed Action**

### ***Continued Examination Under 37 CFR 1.114***

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on April 20, 2009 has been entered.

### ***Amendments***

In the reply filed April 20, 2009, Applicant has cancelled Claims 7-14, 16-17 and 21-22, and withdrawn Claims 2-4, 19 and 24-26.

Claims 2-4, 19 and 24-26 are pending but withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a non-elected invention, there being no allowable generic or linking claim.

This application contains claims, Claims 2-4, 19 and 24-26, drawn to an invention nonelected without traverse in the reply filed on February 12, 2008. Because Applicant did not distinctly and specifically point out the supposed errors in the Group or species restriction requirement, the election was treated as an election without traverse and the restriction and election requirement was deemed proper and therefore made final (MPEP § 818). A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

The Examiner acknowledges Applicant's request to submit Claim 24 for examination. However, the status of Claim 24 remains withdrawn until allowance of the generic claim.

Claims 1, 5-6, 15, 18, 20 and 23 are under consideration.

### ***Priority***

This application is a 371 of PCT/US03/23090 filed on July 24, 2003. Applicant's claim for the benefit of a prior-filed application parent provisional application 60/398,628, filed on July 24, 2002 under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged.

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Accordingly, the effective priority date of the instant application is granted as July 24, 2002.

### ***Information Disclosure Statement***

Applicant has filed Information Disclosure Statements on April 21, 2009 that has been considered. The signed and initialed PTO Forms 1449 are mailed with this action.

The Katz citation (#48) has been lined through because the Examiner has already entered this reference into the record (Office Action mailed May 14, 2008).

### ***Examiner's Note***

Unless otherwise indicated, previous objections/rejections that have been rendered moot in view of the amendment will not be reiterated. The arguments in the April 20, 2009 response will be addressed to the extent that they apply to current rejection(s).

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

5. **Claims 1, 5-6, 15, 18 and 20 stand rejected under 35 U.S.C. 103(a)** as being unpatentable over Handler et al (PNAS 95:7520-7525, 1998) in view of Kim et al (U.S. Patent 6,479,626), Katz et al (Virology 217:178-190, 1996), Elledge et al (U.S. Patent 6,828,093) and Grigliatti et al (U.S. 2002/0116723).

### ***Response to Arguments***

Applicant argues that:

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a) Applicant respectfully submits that a person of ordinary skill in the art would consider transposases, recombinases and integrases to be distinctly different in both evolutionary and mechanistic terms (Coates et al, 2005). The combination of references is based on a premise that is not accepted by the scientific community and which contradicts the Office's own position on the distinction between transposases, recombinases and integrases. A site-specific recombinase does not refer to any enzyme that is a recombinase, a transposase or an integrase but instead refers to a tyrosine recombinase (in which DNA is covalently attached to a tyrosine residue) or to a serine recombinase (in which DNA is covalently attached to a serine residue);

b) Handler does not teach or suggest that the transgene and transposase are on a single nucleic acid construct;

c) Kim is silent with respect to transposases. Thus, Katz does not teach or suggest the chimeric integrating enzyme, which includes a piggyBac transposase-derived integrating enzyme, of the claims;

d) Katz is silent with respect to transposase. Thus, Katz does not teach or suggest the chimeric integrating enzyme, which includes a piggyBac transposase-derived integrating enzyme, of the claims;

e) the disclosure of Elledge is specifically directed to vectors containing the Cre-loxP recombinase system. The reference does not teach or suggest piggyBac transposase, a chimeric integrating enzyme containing a zinc finger-derived DNA binding domain and a piggyBac transposase-derived integrating domain, or a transgene and the recited chimeric integrating enzyme on a single nucleic acid construct; and

f) the disclosure of Grigliatti is specifically directed to vectors containing the P element transposase for use in insect cells. The P element transposase is distinct from piggyBac transposase and, unlike piggyBac transposase, requires insect host cell factors to operate. The only reference to piggyBac transposase is a general statement in Grigliatti regarding the creation of inducible transposase producing cell lines. However, the reference does not teach or suggest piggyBac transposase in a single nucleic acid construct with a transgene, nor does the reference teach or suggest a chimeric integrating enzyme that contains a zinc finger-derived DNA binding domain and a piggyBac transposase-derived integrating domain.

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Applicant's arguments have been fully considered, but are unpersuasive.

With respect to a), the Examiner has performed the factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a). As a first matter, Applicant is respectfully reminded that the Office position to which Applicant refers was prior to search and examination of the claims. As a second matter, the instant specification discloses that the purpose of the invention is for site-selective integration of nucleic acid molecules, achieved via fusion polypeptide comprising a DNA binding domain and any enzyme with integrating capabilities, including but not limited to transposases, integrases, and recombinases (pg 4, lines 2-4; pg 9, [¶51]). Upon a search and examination of the claims, the Examiner has found that those of ordinary skill in the art consider transposases, recombinases and integrases to be species within the same genus of site-specific recombination enzymes. Elledge et al disclosed that site-specific recombinases refers to enzymes that recognize short DNA sequences that become the cross-over regions during the recombination event and includes recombinases, transposases and integrases (col. 17, lines 15-19). Similarly, Coates et al (2005; \*of record in IDS) to which Applicant refers, also teaches that integrases, transposases and recombinases share the same functional property of catalyzing the insertion of foreign DNA into a target nucleic acid (pg 407, col. 2, "tools of the trade"). Thus, both Elledge et al, Coates et al and Applicant recognize transposases, integrases, and recombinases to be enzymes that recognize short DNA sequences that become the crossover regions during the recombination event, thereby integrating a first DNA molecule with another DNA molecule. Regardless of the mechanism, the same functional result is achieved, namely site-specific integration. Thus, at the time of the invention, piggyBac transposase was an art-recognized species within the genus of site-specific recombination enzymes comprising transposases, integrases and recombinases.

With respect to b), in response to Applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In the instant case, Grigliatti et al disclose the transgene and transposase are on a single nucleic acid construct.

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With respect to c-d), in response to Applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In the instant case, Kim et al and Katz et al teach the site-specific recombination enzyme may be a chimeric integrating enzyme. Handler et al and Grigilatti et al teach the integrating enzyme may be piggyBac transposase.

With respect to e), in response to Applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In the instant case, Kim et al and Katz et al teach the site-specific recombination enzyme may be a chimeric integrating enzyme. Handler et al and Grigilatti et al teach the integrating enzyme may be piggyBac transposase. Grigliatti et al disclose the transgene and transposase are on a single nucleic acid construct.

With respect to f), in response to Applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In the instant case, Kim et al disclosed zinc finger-derived DNA binding domains. Kim et al and Katz et al teach the site-specific recombination enzyme may be a chimeric integrating enzyme. Handler et al and Grigilatti et al teach the integrating enzyme may be piggyBac transposase. Grigliatti et al disclose the transgene and transposase are on a single nucleic acid construct.

Furthermore, a reference may be relied upon for all that it would have reasonably suggested to one having ordinary skill the art, including nonpreferred embodiments. *Merck & Co. v. Biocraft Laboratories*, 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), *cert. denied*, 493 U.S. 975 (1989). However, "the prior art's mere disclosure of more than one alternative does not constitute a teaching away from any of these alternatives because such disclosure does not criticize, discredit, or otherwise discourage the solution claimed...." *In re Fulton*, 391 F.3d 1195, 1201, 73 USPQ2d 1141, 1146 (Fed. Cir. 2004). In the instant case, Applicant applies a very

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narrow interpretation of the Grigliatti disclosure. However, the Examiner respectfully reminds Applicant that Grigliatti suggests the use of piggyBac transposase in the same manner in which the P element transposase was used (Grigliatti, [0228-0229]). Thus, it would be reasonable for one of ordinary skill in the art to interpret the transgene and transposase (P-element or piggyBac) are on a single nucleic acid construct [0026].

6. **Claim 23 is rejected under 35 U.S.C. 103(a)** as being unpatentable over Handler et al (PNAS 95:7520-7525, 1998) in view of Kim et al (U.S. Patent 6,479,626), Katz et al (Virology 217:178-190, 1996), Elledge et al (U.S. Patent 6,828,093) and Grigliatti et al (U.S. 2002/0116723), as applied to claims 1, 5-6, 15, 18 and 20 above, and in further view of McFarlane et al (Transgenic Res. 5(3):171-177, 1996; Abstract only).

#### ***Response to Arguments***

Applicant continues to argue that McFarlane et al do not cure the defect of the above cited references

Applicant's argument(s) has been fully considered, but is not persuasive. The Examiner's response to Applicant's argument(s) regarding Handler et al in view of Kim et al, Katz et al, Elledge et al and Grigliatti et al are discussed above and incorporated herein. Applicant does not contest the teachings of McFarlane et al as applied to the obviousness to combine a homologous sequence that is homologous to the host DNA with a nucleic acid composition comprising a transgene flanked by two terminal repeats and a nucleic acid encoding an integrating enzyme under the control of a promoter element with a reasonable chance of success because all the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention.

#### ***Conclusion***

7. No claims are allowed.

This is a RCE of Applicant's earlier Application No. 10/521936. All claims are drawn to the same invention claimed in the earlier application and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the earlier application. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action in this case. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO**



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MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no, however, event will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to KEVIN K. HILL whose telephone number is (571)272-8036. The Examiner can normally be reached on Monday through Friday, between 9:00am-6:00pm EST.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Joseph T. Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Kevin K. Hill/

Examiner, Art Unit 1633

*/Anne Marie S. Weh  /*

Primary Examiner, A.U. 1633